REMARKS

Upon entry of this amendment, claims 10-12, 15, and 19-34 are currently pending in this application. Claim 14 was previously canceled, and claims 1-9, 13, and 16-18 are canceled herein, all without prejudice or disclaimer. Claim 10 is amended herein and new claims 25-34 are added. Support for those amendments can be found throughout the specification, *e.g.*, in the original claims; page 7, lines 16-18 and 29-32; page 8, lines 6-14; page 9, lines 28-30; page 11, lines 20-27; page 11, line 29 through page 12, line 1; page 20, lines 1-3 and 27-30; page 22, lines 24-28; the table bridging lines 28-29 on page 12; the table bridging lines 12-13 on page 17; and in Examples 1, 2, and 4 on pages 9-14 and 16-18. Thus, no new matter has been added.

CLAIM OBJECTIONS

The Office objects to claim 13 "because the concentration in line 4 of claim 13 should be expressed in 'g/l.'" (Office Action at p. 2.) Claim 13 is canceled herein without prejudice or disclaimer, rendering this objection moot.

REJECTION UNDER 35 U.S.C. § 112 - NEW MATTER

Claim 13 is rejected under 35 U.S.C. § 112, ¶ 1 as allegedly containing new matter. (Office Action at pp. 8-9.) Specifically, the Office contends that "the specification does not provide information in regards to any amino acids having concentration from about 67 to about 110 g/l, but only has information in regards to glycine that can have such concentration. Further, specification does not teach that any alkali metal or alkaline earth metal salt has concentration of 100 to 160 g/l, but only has

information in regards to NaCl that can have such concentration." (*Id.*) Applicant respectfully traverses.

Claim 13 is canceled herein without prejudice or disclaimer, rendering this rejection moot. However, currently amended claim 10 recites "wherein the fractional concentration of the amino acid is from about 67 to about 110 g/l and the fractional concentration of the alkali metal or the alkaline earth metal salt is from about 100 to about 160 g/l," and new claim 25 recites "wherein the fractional concentration of the amino acid is from 67 to 110 g/l and the fractional concentration of the alkali metal or the alkaline earth metal salt is from 100 to 160 g/l." Thus, Applicant will address this rejection as it might apply to these claims.

With regard to the fractional concentration of the alkali metal or alkaline earth metal salt, currently amended claim 10 recites the range "from about 100 to about 160 g/l," and new claim 25 recites the range "from 100 to 160 g/l." The Office contends that the specification "only has information in regards to NaCl that can have such concentration" and "does not teach that any alkali metal or alkaline earth metal salt has concentration of 100 to 160 g/l." (Office Action at pp. 8-9; emphasis added.) However, claim 13 of the originally filed application recited "the fractional concentration of the alkali metal or the alkaline earth metal salt is from 100 to 160 g/l." (Original claim 13, emphasis added.) This element has been incorporated word-for-word into new claim 25, and a modified version has been incorporated into currently pending claim 10. As is well established, "a satisfactory description may be in the claims or any other portion of the originally filed specification." (M.P.E.P. 8th Ed., 6th. Rev.; *see also In re Gardner*, 480 F.2d 879, 880 (C.C.P.A. 1973) ("we consider the original claim in itself adequate

'written description' of the claimed invention.").) Thus, the originally filed specification provides adequate support for the fractional concentrations of alkali metal or alkaline earth metal salts recited in claims 10 and 25.

With regard to the fractional concentration of amino acid, currently amended claim 10 recites the range "from about 67 to about 110 g/l," and new claim 25 recites the range "from 67 to 110 g/l." Applicant acknowledges that the specification does not literally recite these ranges of fractional concentrations of amino acid. However, "ranges in applicant's claims need not correspond exactly to those disclosed in the [specification]." *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 1001 (Fed. Cir. 2000) (citing *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985)). Rather, the proper inquiry is "whether one of skill in the art could derive the claimed ranges from the [specification]." *Id.* Indeed, "[i]f lack of literal support alone were enough to support a rejection under § 112, then the statement of *In re Lukach* . . . that 'the invention claimed does not have to be described *in ipsis verbis* in order to satisfy the description requirement of § 112' is empty verbiage." *In re Wertheim*, 541 F.2d 257, 265 (C.C.P.A. 1976).

In *Wertheim*, the claims at issue were directed to a process for making freeze-dried instant coffee containing a range of solids content of "between 35 and 60%." The BPAI held that the claims were not supported by the specification, which disclosed a broader range of 25 to 60%. The CCPA reversed, holding that the specification supported the claimed range even though the precise range of the claim was not repeated verbatim in the specification because "as a factual matter, persons skilled in the art would consider processes employing a 35-60% solids content range to be part of

appellants' invention." *Wertheim*, 541 F.2d at 265. The court noted that "applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable" and that the law "does not prohibit the applicant from changing what he 'regards as his invention' (*i.e.*, the subject matter on which he seeks patent protection) during the pendency of his application." *Id.* at 263. The court cautioned that "[t]o rule otherwise would let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed." *Id.*; *see also Union Oil*, 208 F.3d at 1000.

Here, as in *Wertheim*, Applicant has narrowed a range recited in the specification based on the operable embodiments disclosed in the Examples. For instance, the specification discloses several exemplary precipitations using amino acid concentrations of 66.7, 71.1, 80, 90, 90.4, 100, and 109.6 g/l, all of which produced vWF:RCoF/vWF:Ag ratios greater than 1. (*See* Example 1 at p. 10, ll. 16-18 and Table 1; Example 2 at p. 12, ll. 28-30 and Tables 3 and 4; and Example 4 at Tables 7 and 8.) Thus, as in *Wertheim*, one of skill in the art could readily derive the range of operable amino acid concentrations recited in currently pending claims 10 and 25 from the broader range recited in the specification based on the working examples.[1]

[1] As discussed in the Amendment and Response filed July 14, 2008, one skilled in the art would understand that since the currently pending claims recite whole numbers, Examples 2 and 4 illustrate that Applicant was in possession of fractional concentrations of amino acid of 67 and 110 g/l because 66.7 and 109.6 g/l round to the whole numbers 67 and 110 g/l, respectively. *See* Amendment and Response filed July 14, 2008, at p. 12.

The Office contends, however, that "the specification does not provide information in regards to any amino acids having concentration from about 67 to about 110 g/l, but only has information in regards to glycine that can have such concentration." (Office Action at p. 8; emphasis added.) Applicant respectfully disagrees. Original claim 13 recited "the fractional concentration of the amino acid is from 70 to 160 g/l" (original claim 13, emphasis added), and modified versions of this element have been incorporated into currently pending claims 10 and 25. As discussed above, "a satisfactory description may be in the claims or any other portion of the originally filed specification." (M.P.E.P. 8th Ed., 6th. Rev.) Thus, the originally filed specification provides adequate support for the fractional concentrations of amino acid recited in claims 10 and 25.

Here, as in *Wertheim*, the range recited in the currently pending claims covers the invention to which Applicant is entitled. In the Response filed July 14, 2008, Applicant explained that one of the inventive features of this application is the unexpected discovery that the concentration of amino acid used in the fractional precipitation affects whether the resulting concentrate exhibits a vWF:RCoF/vWF:Ag ratio greater than 1. For example, the specification teaches that "partitioning of the vWF multimers according to size can be achieved by appropriate adjustment of the equilibrium" between the alkali metal or alkaline earth metal salt and amino acid (page 22, lines 24-27, emphasis added), and Examples 1-4 demonstrate that fractional precipitations using concentrations of amino acid greater than about 110 g/l produced vWF:RCoF/vWF:Ag ratios less than 1, whereas ratios greater than 1 were consistently observed when the fractional concentration of amino acid was from about 67 to about

110 g/l. (*See also* Exhibit A filed with the Response dated July 14, 2008.) Thus, Applicant has discovered that vWF/FVIII:C concentrates having vWF:RCoF/vWF:Ag ratios greater than 1 reproducibly result from precipitations using fractional concentrations of amino acid from about 67 to about 110 g/l. Currently amended claim 10 and new claim 25 recite that inventive feature of the application. Since one skilled in the art could readily derive the claimed ranges of amino acid concentrations from the teachings of the specification, Applicant should not be prohibited from claiming such ranges merely because the specification recites a broader range of amino acid concentrations.

For at least these reasons, the currently pending claims are fully supported by the originally-filed specification. Accordingly, Applicant respectfully requests that the new matter rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112 - ENABLEMENT

Claims 10-13, 15, and 19-24 are rejected under 35 U.S.C. § 112 ¶ 1 as allegedly failing to comply with the enablement requirement. (Office Action at pp. 2-8.) Specifically, the Office contends that Heimburger V. N. et al., "Factor VIII Concentrate, Highly-Purified and Heated in Solution," Drug Res., 31:619-622 (1981) ("*Heimburger*") "clearly teaches the same method that utilizes the same steps where the ratio for the same compositions is less than 1" and concludes that "there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented." (*Id.* at p. 4.) Applicant respectfully traverses.

Claim 13 is canceled herein without prejudice or disclaimer, rendering the rejection of that claim moot. With respect to the remaining claims, independent claim 10, from which claims 11, 12, 15, and 19-24 depend, is amended herein to recite "wherein the fractional concentration of the amino acid is from about 67 to about 110 g/l and the fractional concentration of the alkali metal or the alkaline earth metal salt is from about 100 to about 160 g/l," and new claim 25, from which claims 26-34 depend, recites a similar limitation without the term "about." Applicant submits that the specification fully enables one skilled in the art to practice the invention of the currently amended claims.

On pages 3-4 of the Office Action, the Office addresses each of the factors set forth in *In re Wands* for determining whether a disclosure satisfies the enablement requirement. *See In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988). The Office acknowledges that the nature of the invention is a fractional precipitation method for producing a concentrate of a factor VIII:C-containing von Willebrand factor using an alkali metal salt and an amino acid chosen from glycine, α- or β-alanine, α-, β-, or γ-aminobutyric acid, lysine, valine, asparagine, and glutamic acid, wherein the concentrate has an increased content of high molecular weight multimers of vWF and a ratio of von Willebrand factor ristocetin cofactor activity to von Willebrand factor antigen of greater than 1 (*see* Office Action at page 3), and that the level of skill in the art is high (*see* Office Action at page 4).

However, in analyzing the breadth of the claims, the Office contends that "the claims are broad because they refer to a process for producing a concentrate of factor VIII:C-containing von Wilebrand factor (vWF/FVIII:C) wherein the concentrate has a ratio of vWF:RcoF [sic] to vWFAg of greater than 1." (Office Action at p. 3.) Applicant

respectfully disagrees and submits that the Office has improperly based its conclusion regarding the breadth of the claims on only one of the claim elements. As a result, the Office has failed to consider that the claims are also limited to: (1) alkali metal salts or alkaline earth metal salts; (2) amino acids chosen from glycine, α- or β-alanine, α-, β-, or γ-aminobutyric acid, lysine, valine, asparagine, and glutamic acid; and (3) concentrates having an increased content of high molecular weight multimers of vWF. In addition, claims 10-12, 15, and 19-24 are limited to fractional precipitations "wherein the fractional concentration of the amino acid is from about 67 to about 110 g/l and the fractional concentration of the alkali metal or the alkaline earth metal salt is from about 100 to about 160 g/l," while claims 25-34 are limited to fractional precipitations "wherein the fractional concentration of the amino acid is from 67 to 110 g/l and the fractional concentration of the alkali metal or the alkaline earth metal salt is from 100 to 160 g/l." Accordingly, Applicant respectfully submits that the scope of the claims is not overly broad when all of the claim elements are considered.

Regarding the amount of direction provided by the specification and the existence of working examples, the Office contends that these *Wands* Factors are limited to "working examples 1 and 2 and Table 1 on pages 10 and 11" of the specification. (Office Action at p. 4.) Applicant respectfully disagrees and submits that the Office has failed to include the teachings of Examples 3-5 and Tables 3, 4, 6, 8, and 9 on pages 14-21 of the specification. These Examples and Tables disclose additional embodiments of the invention in which the resulting concentrate has a vWF:RCoF/vWF:Ag ratio greater than 1, as well as inoperable embodiments in which the vWF:RCoF/vWF:Ag ratio is less than 1. In total, the specification provides **ten**

examples of operative embodiments of the invention and **ten** examples of inoperative embodiments. Accordingly, Applicant respectfully submits that the specification provides sufficient working examples and direction to allow one skilled in the art to practice the claimed invention.

In analyzing the level of predictability in the art, the state of the prior art, and the quantity of experimentation needed to make or use the invention, the Office contends that *Heimburger* illustrates the state of the prior art and establishes that "the instant invention is unpredictable because the instant method claimed does not produce a concentrate in which the ratio of ristocetin to vWF is greater than 1 because the prior art reference teaches that the same method steps produce a concentrate in which the ratio is less than 1." (Office Action at p. 4.) The Office also contends that "there is a large quantity of experimentation necessary to determine whether the method claimed . . . is actually claimed since the prior art by Heimburger et al. clearly teaches the same method that utilizes the same steps where the ratio for the same compositions is less than 1." (*Id.*) Applicant respectfully disagrees.

As discussed above, claim 10 is amended herein to recite that the fractional concentration of amino acid is "from about 67 to about 110 g/l," and new claim 25 recites that the concentration of amino acid is "from 67 to 110 g/l." In contrast, *Heimburger* uses an amino acid concentration of 128.3 g/l, which is outside the range recited in the currently pending claims. (*See* Declaration of Gerhardt Kumpe Under 37 C.F.R. § 1.132 dated February 25, 2008, at ¶ 8.) However, the Office contends that "'about 110 g/l' would include numerical values that are greater than 110 g/l and thus being in the range taught by Heimburger." (Office Action at p. 6; *see also* p. 7

("Heimburger teaches concentration of glycine of greater than 110 g/l and the instant invention claims amino acid concentration of about 110 g/l, thus the numerical values [are] in the same range.").) Applicant respectfully disagrees.

"The use of the word 'about,' avoids a strict numerical boundary to the specified parameter" and its "meaning depends on the technological facts of the particular case." *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Lab., Ltd.*, 476 F.3d 1321, 1326 (Fed. Cir. 2007) (citing *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995). When interpreting the range encompassed by the term "amount" in a claim, "[i]t is appropriate to consider the effects of varying that parameter, for the inventor's intended meaning is relevant." *Id.* (emphasis added). Here, the specification demonstrates that when the amino acid concentration used in the fractional precipitation is varied by at least 17% above the range recited in the currently pending claims, the resulting concentrates consistently have vWF:RCoF/vWF:Ag ratios less than 1. (*See* Example 2 at p. 12, ll. 22-24 and Table 4; Example 3 at Tables 5 and 6; and Example 4 at Tables 7 and 8; *see also* Exhibit A filed with the Response dated July 14, 2008.) Thus, the specification provides a clear indication of the range encompassed by the term "about 110 g/l" in currently amended claim 10. Indeed, the 128.3 g/l amino acid concentration used in *Heimburger* was tested **five** times and produced vWF:RCoF/vWF:Ag ratios less than 1 each time. (*See* Example 3 at Tables 5 and 6; and Example 4 at Tables 7 and 8.) Thus, based on the working examples in the specification, one skilled in the art would understand that *Heimburger*'s amino acid concentration of 128.3 g/l is not encompassed by the term "about 110 g/l" in the currently pending claims. Accordingly, *Heimburger* does not "teach the same process

for producing a concentrate that utilizes the exactly same steps" as the claimed invention (Office Action at p. 7) and, therefore, one skilled in the art would not expect the method disclosed in *Heimburger* and the instantly claimed method to produce the same results. In fact, rather than calling the operability of the instant invention into question, *Heimburger* supports Applicant's discovery that fractional concentrations of amino acid greater than about 110 g/l do not produce vWF:RCoF/vWF:Ag ratios greater than 1. Thus, the level of predictability in the art and the state of the prior art confirm that the claimed invention does not require undue experimentation.

For at least these reasons, the instantly claimed invention is fully enabled by the originally filed specification. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. § 112 ¶ 1 be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: January 30, 2009

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